

Application No. 10/714,447  
Amendment Dated November 30, 2005  
Reply to Office Action of September 9, 2005

### Remarks

No amendment is made in this response to the Final Rejection. Claim 19 is pending.

In the Office Action, claim 19 was rejected under 35 U.S.C. § 103 (a) in view of Chang et al (PCT Publication WO93/15062 or U.S. Pat. No. 5,658,908, applied as of its § 102(e) date). Applicant respectfully traverses the rejection for the following reasons.

First of all, Applicants submit that claim 19 is patentable in view of Chang et al because Chang et al expressly teaches away from claim 19. A prior art that teaches away from claimed invention is a significant factor to be considered in determining obviousness. MPEP §2146.1. References cannot be combined where references teaches away from their combination. MPEP §2146.2. In addition, a prior art reference must be considered in its entirety, including disclosures that teach away from the claims. MPEP §2141.02

In this case, Chang et al teach that it is important to have the substitution on the piperazine ring. See page 60 of the comments made during a response by Chang et al on February 9, 1996 (a 132 declaration filed by Chang et al) during the prosecution of Chang et al., copies of the relevant pages are attached as Appendix I for the convenience of the Examiner. In the response, Chang et al made the following statements:

Specially, these tests included four pairs of compounds, in which one of the two compounds, like all of the compounds disclosed in Iwamoto I and II, had no substituents on carbon atoms of the piperazine ring. The other compound of the pair was the same as the first, except that it had two methyl groups on carbon atoms of the piperazine ring is substituted with two methyl groups, with those that do not have a substituent on any of the carbon atoms of the piperazine ring, show a general trend in which the substituted compounds have significantly greater opioid activity.

The file wrapper is considered an integrated part of Chang et al. A person skilled person reading Chang et al as a whole would be motivated to combine Chang et al and Brown et al in such a way that it would not arrive at the present invention because the skilled person would not only change the functional groups of Brown et al as suggested by the Examiner but also introduce the methyl groups onto the piperazine ring as specifically taught by Chang et al. Therefore, the motivation to combine Chang et al and Brown et al to arrive at the present invention is lacking for this reason.

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In addition, Applicants repeat the arguments advanced in our response dated June 17, 2005 in the instant application and submit that the pending claim is patentable for those additional reasons.

Having now responded to all the rejections, Applicants believe the application is in condition for allowance, which action is respectfully requested.

Although Applicants believe no fees are due, the Commissioner is hereby authorized to charge any deficiency in the fees or credit any overpayment to deposit account No. 26-0166, referencing Attorney Docket No. A1479-3P US.

Respectfully submitted,

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Enclosures: Copies of Response filed by Chang et al.